FDA Public Health Web Notification[1]: Updated Information for Physicians on Sub-acute Thromboses (SAT) and Hypersensitivity Reactions with Use of the Cordis CYPHER™ Sirolimus-eluting Coronary Stent

Issued 11/25/2003

Our October 29, 2003, Web Notification regarding the association of sub-acute thromboses (SATs) and hypersensitivity reactions with the CYPHER™ Stent advised you of reports we received through the Medical Device Reporting (MDR) system. We want to be sure physicians and their patients understand that, based on the information currently available, we consider the CYPHER™ Stent a safe and effective product when used according to the labeling, particularly concerning patient selection and appropriate peri-procedural medications.

FDA's Role

One role of the Food and Drug Administration (FDA) is to follow products once they have been approved or cleared for marketing. We monitor any new technology after approval, especially one used in a vital organ such as the heart. We do this to understand how the device is being used in the general medical community and what adverse events are occurring to ensure that the product continues to be safe and effective for its labeled indication. During its initial release in April 2003, the CYPHER™ Stent had widespread adoption. During that same period, a small number of hospitals reported a higher than expected number of thromboses. With our primary focus on patient safety, we have closely monitored all reported adverse events to determine whether these events were widespread and to determine if there was any pattern that would explain these events. On July 7, 2003, Cordis Corporation provided initial information in a "Dear Colleague" letter. On October 29, 2003, we shared additional information with you in our Web Notification.

Sub-acute Thrombosis

Sub-acute thrombosis is a relatively rare event that occurs within the first 30 days following the stenting procedure and can occur with any stent, bare metal or a drug-eluting stent. The rate of sub-acute thrombosis associated with any stent is highly dependent on the population in which they are used. Reports received through the MDR system, which is subject to significant

[1] CDRH Web Notifications are intended to augment the existing Safety Notification program by providing a mechanism to quickly disseminate device–related safety information that may be beneficial to healthcare providers. Unlike other forms of Notifications, such as Safety Alerts or Public Health Advisories, Web Notifications usually do not make specific recommendations and are typically used in situations where the available information and our understanding of an issue are still evolving.

underreporting, reflect use of the CYPHER™ stent in a diverse population. Between October 20 and November 22, 2003, we have received 75 additional MDR reports (for a total of more than 360 to date) of SAT associated with the CYPHER™ stent. In the same time period, Cordis has distributed about 125,000 CYPHER™ stents (more than 575,000 to date). Based on our review of data supporting the CYPHER™ stent from clinical trials (some of which included treating more complex lesions), it appears that the rate of SATs is within the expected rate for any stent.

Hypersensitivity

Another area we have monitored is reports of hypersensitivity reactions. In most cases reported to FDA, hypersensitivity seen with implantation of the CYPHER Stent was minor (e.g., skin rashes and itching that cleared up within a few days of onset), but there were some severe reactions (including anaphylaxis). Although some of the reactions we have observed so far remain unexplained, many of the reactions are believed to be events related to standard drug therapy associated with the procedure. Between October 20 and November 22, 2003, we have received 20 additional MDR reports (more than 70 to date) of hypersensitivity associated with the CYPHER™ stent, with no additional deaths.

Ongoing Efforts

Cordis Corporation is currently conducting a 2,000 patient post-approval registry as part of its conditions of approval. They expect to provide us with the initial results of this registry in early 2004. As we wait for these data, we will continue to monitor all reported events for the CYPHER™ Stent, as we do with all medical devices.

We are continuing to evaluate all available information from the MDR reports as well as other sources. We will provide updates on the numbers of MDR reports we receive on SATs or hypersensitivity associated with the CYPHER stent as warranted. We will also advise you of any new information that may be of use in the selection or treatment of your patients as it becomes available.

Reporting to FDA

The Medical Device Reporting (MDR) regulation, 21 CFR Part 803, **requires hospitals and other user facilities, as defined by Part 803.3, to report adverse events to FDA and the device manufacturer** when the event is associated with the use of the medical device and the device may have caused or contributed to a patient death or serious injury. You may refer to our MDR web site at: http://www.fda.gov/cdrh/mdr/.

You can also report to MedWatch, the FDA's voluntary reporting program. You may submit reports to MedWatch one of four ways: online at http://www.accessdata.fda.gov/scripts/medwatch/; by telephone at 1-800-FDA-1088; by FAX at 1-800-FDA-0178; or by mail to MedWatch, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

FDA Contacts

Laura Alonge
Office of Surveillance and Biometrics (HFZ-510)
1350 Piccard Drive, Rockville, Maryland, 20850
Fax at 301-594-2968, or by e-mail at phann@cdrh.fda.gov.

Additionally, a voice mail message may be left at 301-594-0650 and your call will be returned as soon as possible.